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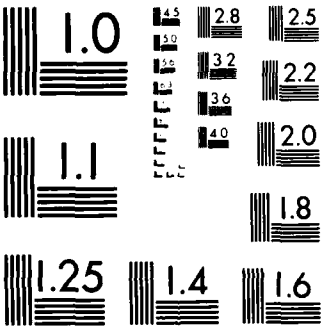

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LASSA FEVER IMMUNE PLASMA

Annual Summary Report

John D. Frame, M.D.

August, 1984

Supported by

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Frederick, Maryland 21701-5012

Contract No. DAMD17-79-C-9024

Trustees of Columbia University
In the City of New York
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

One hundred forty-one Lassa Fever Immune Plasma (LFIP) Units have been obtained by plasmapheresis in the last 12 months; 59 have been forwarded to USAMRIID and 16 more are awaiting shipment to the United States. Virological and serological testing for Lassa fever (LF) at Curran Lutheran Hospital and at Phebe Hospital has identified 51 cases of LF and 86 of presumptive LF at the two institutions. LV was isolated from 16 of these patients.

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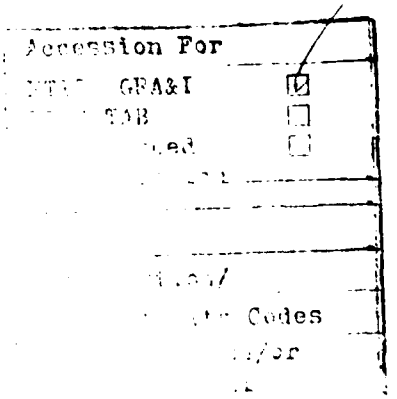
Surveys for the prevalence of LF has been conducted at Taninahun and Kondonbengu, in Lofa County, with prevalences of 2.1% and 2.5% found in them, respectively. The prevalences in these "bush" villages may be compared with an average of 4.7% in two roadside villages in the same district surveyed a year ago.

The use of LFIP in the treatment of patients under controlled conditions has been started at CLH; virus isolation to monitor the success of treatment have not been completed so far.



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Summary

During the past year 141 Lassa Fever Immune Plasma (LFIP) Units were obtained by plasmapheresis at the Curran Lutheran Hospital (CLH) in Zorzor, Liberia. Fifty-nine units have been forwarded to the United States Army Medical Research Institute of Infectious Diseases, and 16 others are awaiting transportation to the USAMRIID.

The identification of Lassa fever (LF) patients among fever cases at CLH and at Phebe Hospital, Bong County, continued. 40 LF and 63 presumptive LF patients were identified out of 50 tested at CLH, and 11 LF and 23 presumptive LF among 199 patients at PH. Lassa virus (LV) was isolated from patients. Virus isolation has not yet been completed in 229 patients at CLH and 95 at PH.

A serological survey of patients was conducted in June, 1984 at the Leprosy Hospital in Ganta, Liberia. Testing of sera has not been completed at the time of this report.

Village surveys were conducted to determine the prevalence of LV antibodies in two villages, Taninahun and Kondonbengu, in Kolahun District, Lofa County.

Treatment of patients with LFIP has been started under controlled conditions at CLH, but appropriate virological testing to determine the results of treatment have not been completed.

Mr. J.E. Yalley-Ogunro, Field Investigator and Resident Head, and Andrew Cole, M.D., Clinical Investigator, both Liberians, conduct the work in Liberia, under the general direction of John D. Frame, M.D., Principal Investigator. The latter traveled to Liberia in April, and expects to return in October of this year.

FORWARD

For the protection of human subjects the investigator(s) have adhered to policies of applicable Federal Law 45CFR46.

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I. Statement of the Problem

Lassa fever (LF), was first found in nosocomial outbreaks in Nigeria, Liberia and Sierra Leone[1,2,3,4]. Lassa virus (LV) infections have since been found to be widespread throughout West Africa[5]. Treatment has generally been supportive; in addition, specific treatment with LF Immune Plasma (LFIP) has been used with good results when given early in the course of the illness[6,7].

Prevention of LF requires elucidation of its epidemiology, and will likely require the preparation and use of a vaccine. However, investigations into LV infection carry a definite risk[8], and LFIP is needed to protect investigators as well as patients. Thus, research into the epidemiology and pathogenesis of LF, in the nature of the virus, and in the development of a preventive vaccine appear to be of high priority if this hemorrhagic fever is to be brought under control.

II. Background

The background of LF research in Liberia has been covered extensively in Annual Summary Report, August 1983. In brief, LF was first identified in Liberia in 1972[3] and research starting in 1976 demonstrated high prevalences of LV antibodies (LVA) among staff members of Liberian hospitals[9]. The Republic of Liberia agreed to ongoing research in LF. A joint program to procure LFIP and to study the epidemiology of LF was entered upon by Columbia University (CU), and the Liberian Institute for Biomedical Research (LIBR) and the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) under Contract DAMD 17-79-C-9024 awarded by the U.S. Army Medical Research and Development Command.

Early in the collection of LFIP it became apparent that timing of plasmapheresis several months into convalescence ensured adequate levels of neutralizing antibody (NA) as determined by the Log Neutralization Index[10]. By August 1983 154 units of LFIP meeting the criteria of USAMRIID based on appropriate LNI's had been collected and 110 forwarded to USAMRIID, the balance being left in Liberia for treatment of patients there.

LF has been found to be the cause of illness in 10 to 15% of adult patients with fever admitted to hospitals in northwestern Liberia[11,12]; it is among the most common causes of fever in the hospitals. LV activity has been demonstrated throughout Liberia, a determination based on the survey of hospital staffs in all counties but one[13]. Numerous isolates of LV have been made from patients at the Curran Lutheran Hospital (CLH), Lofa County, and Phebe Hospital (PH), Bong County. Surveys of 8 villages in Lofa County have demonstrated prevalences of LVA

ranging from 0.9% to 14.1%.

III. Approach to the Problem

Plasma donors were identified by continued serological testing of febrile patients in hospitals, and by virus isolation. Potential donors were requested to submit sera for testing for LV NA, and those with adequate LNI were asked to submit to plasmapheresis.

Patients who on clinical grounds were considered to have LF were treated with LFIP, and their course monitored by clinical, biochemical and virological measures.

Epidemiological investigations were carried out among patients found to have LF, and by means of village surveys for the prevalence of LF; villages were selected for differences among them that might elucidate factors contributing to the varying prevalences of LF.

IV. General Narrative

Throughout the year Mr. J. E. Yalley-Ogunro, the Field Investigator and Resident Head of the project in Liberia, traveled repeatedly from his base at the LIBR at Robertsfield to CLH to conduct plasmapheresis, and to collect sera obtained from febrile patients at CLH, PH and Kolahun in Lofa County. Upon his return to his laboratory at the LIBR he tested specimens for indirect fluorescent antibodies (IFA) by means of the fluorescence microscope there, using antigen spot slides supplied by USAMRIID.

In October, 1983 and April, 1984, the Principal Investigator, John D. Frame, M.D., traveled to Liberia. He visited PH and CLH to review the collection of patient sera there, and supervised the induction of laboratory technicians at CLH and PH into systematic serum collection. He traveled with Mr. Yalley-Ogunro to Kolahun, 100 miles west of CLH, to review the work of Dr. Andrew Cole, the Clinical Investigator, and with him in April visited the Swedish Free Pentecostal Mission Clinic (SMC) in Foya Kamara, another 40 miles west and on the Sierra Leone border.

Together with the Field Investigator, Dr. Frame conducted plasmapheresis at CLH, on both visits. He consulted with the Director of the LIBR, Aloysius P. Hanson, Ph.D., on administrative matters relating to the investigations in Liberia, and with Walter Gwenigale, M.D., and John Fredell, M.D., Director and Chief Medical Officer, respectively, at PH regarding the extension of research in that institution.

Dr. Cole and Mr. Yalley-Ogunro conducted surveys in two other villages in Kolahun District, and in the Leprosy Village near Ganta, in Nimba County.

Early in 1984 ultra-freezers were sent to CLH and PH, and a refrigerated centrifuge to PH. Beginning in February, 1984 a program of close monitoring of patients by clinical, biochemical and virological means was established at CLH, in order to ascertain more accurately the results of treatment with LFIP there. At PH the new equipment was installed to permit plasmapheresis for the collection of LFIP.

V. Results

A. Plasmapheresis

During the year plasma was obtained from LF convalescents at least three months after the onset of their illness. It has previously been determined by Jahrling of the USAMRIID that NA as determined by LNI did not reach appropriate levels for their use in the treatment of patients until three to nine months after an attack of LF. Plasmapheresis for LFIP was in most instances conducted six or more months after the onset of LF.

Since the previous Annual Summary Report dated August, 1983 141 units of LFIP have been obtained by plasmapheresis at the Curran Lutheran Hospital, with collections made September, October and December, 1983 and February, April and June, 1984. All but two units were found to meet the criteria for acceptable antibody titers, at an LNI 0.3. Fifty nine units of LFIP were forwarded to USAMRIID and 16 are waiting transportation. 66 units have been kept in Liberia for the treatment of patients there.

An LNI of 2.1 is considered necessary if the LFIP units are to be used directly in the treatment of patients. 56 units meet this criterion; they were obtained from 12 of the 29 donors. The remaining LFIP units submitted to USAMRIID are to be processed to Lassa Fever Immune Globulin of sufficent antibody titer to be useful in the treatment of patients.

Plasmapheresis at PH has been delayed by problems in the electrical circuitry. The appropriate electric wiring to a 220-v circuit suitable for the refrigerated centrifuge has now been completed. 20 units of LFIP were obtained in July; they remain to be tested at USAMRIID to determine their suitability for use in the treatment of LF patients.

The LFIP units, their IFA titers and LNI are listed in the Table, Appendix A.

B. Hospital patients

The virological and serological testing of febrile hospital patients for LF has continued. The diagnosis of "Lassa Fever" has been made on the basis of virus isolation, or by

seroconversion or a 4-fold rise in LVA as determined by the IFA technique. "Presumptive Lassa Fever" has been diagnosed by the presence of titers of LVA of 1:64 or more, either on single specimens or in both members of serum pairs. The results of tests are incomplete to the extent that recent shipments of specimens have not yet been tested virologically at USAMRIID.

Virus isolation has been performed at USAMRIID. Serological testing was done at the laboratory at the LIBR; during this year parallel tests of LVA titers to their end points were in many specimens not carried out at USAMRIID, so that the titers listed are those of the LIBR laboratory. Previous experience has demonstrated good congruence between IFA testing at the LIBR and USAMRIID.

1. Curran Lutheran Hospital

Virus isolation was conducted at USAMRIID on 58 patients reported last year in whom the procedure had not been completed at the time of the Annual Summary Report, dated August, 1983. Both virological and serological tests were completed in another 214 patients, and serological tests only in 229 patients in CLH between December, 1983, and April, 1984.

LV was isolated from 12 of the 272 patients subjected to complete testing, and LF was diagnosed on the basis of seroconversion or a rise in LVA titers in another six. Presumptive LF was diagnosed in nine patients for a total of 27 cases of LF or presumptive LF, 10% of the cases of fever. Of those tested only for LVA, 22 showed seroconversion or 4-fold rises in antibody titers, and another 14 high LVA titers compatible with the diagnosis of presumptive LF. The 36 cases in all were 15.7% of the fever patients.

The incidence of LF among febrile patients in Liberia has been uncertain, even in CLH where attempts have been made to test all patients suspected as possible LF patients. Because of the pressure of the hospital's clinical needs the laboratory has at times been unable to follow up all patients in the hospital with fever with serial serum samples. In the spring of 1983 two laboratory technicians at CLH were given the specific responsibility of obtaining appropriate specimens, and between April, 1983 and March, 1984, tests were performed rather completely, except during the single month of June, 1983. Virus isolation has not yet been completed on 229 of the 447 patients tested during the year. LF or Presumptive LF was diagnosed in 55 patients, an incidence of 12.5%. Previous experience (see below) suggests that 6 or 7 more cases will be added to the number when virus isolation has been performed, for a total of over 60 cases during the year.

Of the 55 cases discovered so far, clinical information has been received for 46. Among 14 adult males there were two

deaths, for a case fatality rate of 14.3%. There were 26 cases and two deaths among women, with a case fatality rate of 7.7% among them. There were no deaths among childhood cases. The case-fatality rate of all 46 patients was 8.7%.

As familiarity with the clinical appearance of LF increases the staff is increasingly able to diagnose LF on clinical grounds, and did so in 38 of the 46 cases. Other clinical discharge diagnosis of LF patients, made before the results of specific laboratory tests were at hand, were typhoid fever in three instances, and one each for sickle cell crisis, severe anemia, pyelonephritis, cerebral malaria and tonsillitis.

Treatment of LF with LFIP under controlled conditions was started early in 1984 at CLH. The response to treatment will be measured by determination of the degree of viremia. Virus isolation has not yet been completed on the pre- and post-tretment serum specimens obtained.

2. Phebe Hospital

The testing of patients for LF at PH has been conducted in a generally random way since mid-1981. It has suffered from poor oversight, incomplete collection of serum pairs and inadequate refrigeration. In December, 1983 a technician was obtained who would devote his time to the collection of sera from suspected LF patients and to assist in the plasmapheresis of LF convalescents. In February an ultra-cold freezer was installed. The results of the testing of febrile patients at PH reflects the relatively unsatisfactory conditions prevailing prior to these changes.

In the previous Annual Summary Report, dated August, 1983 the results of serological tests performed among 104 patients surveyed prior to February 1983 were given; virological testing has been carried out on these since then. LV has been isolated from four, and LF diagnosed serologically on another five. Four other patients had high serum titers of LVA compatible with the diagnosis of presumptive LF, for a total of 13, or 12.5% of the patients treated for fever.

Virus isolation has not been completed in another 103 patients tested between March, 1983 and mid-April, 1984. Serum pairs were obtained in 14 instances; seroconversion was recorded in two. Five patients had high LVA titers compatible with presumptive LF.

3. Leprosy Hospital, Ganta

A survey of patients at the Leprosy Hospital in Ganta, Nimba County was performed in June. Serological testing has not yet been completed for this group.

4. Comparison of virological and serological techniques in the diagnosis of LF.

Appendix C. Surveys of Taninahun and Kondonbengu, Kolahun District, Liberia, for prevalences of LVA determined by the IFA technique.

In the spring of 1984 the populations of these villages were tested for the presence of antibodies to LV. Taninahun and Kondonbengu are located off the main highway, though the latter is on a secondary through road to Foya Kamara.

Table C-1 indicates the number sera positive by titer. The prevalence of LVA was essentially the same in both villages, though in Kondonbengu there were a number of sera with relatively high antibody titers suggesting recent experience with LV among its inhabitants.

Table C-2 demonstrates no difference in the presence of LVA between males and females. The prevalence of antibodies was highest among adults.

Table C-3 compares the LVA prevalences between these two villages which were located off the main highway with Mbabahun and Korworhun, two communities surveyed last year which were both on the highway. The prevalence of LVA was twice as high in the roadside villages as in those "in the bush", but the difference in this comparison was not quite statistically significant.

Table C-1. Prevalence of LVA among inhabitants of two villages in Kolahun District, Lofa County, Liberia by IFA titers.

Village	No. Tested	No. positive by antibody titer						Total Positive		Quest-ionable
		1:8	1:16	...	1:256	1:512	... 1:2048	No.	Rate(%)	
Taninahun	236	4	1					5	2.1	13
Kondonbengu	239	2	1		1	1	1	6	2.5	11

Table B-4. Comparison of virological and serological techniques in the diagnosis of LF at the Curran Lutheran Hospital, Zorzor,Liberia

	Lassa Fever:			Presumptive LF: High LV Titers	Total
	Virus Isolation	Seroconversion of rising antibodies	Total cases		
Diagnosed by:					
Virus isolation only	17		17		17
Virus isolation and Serology	25	16	25	9	25
Serology only		40	40	28	68
Total	42	56	82	37	110

Total LF: 82 cases; total LF + presumptive LF: 110 cases.

Virus isolation: 42/82 or 51.2% of LF cases; 42/110 of 38.2% of LF + presumptive LF cases.

Serological positives: 56/82 or 68.3% of LF cases; 93/110 or 84.5% of LF + presumptive LF cases.

Table B-2. Distribution, by age and sex, 46 LF and Presumptive LF patients treated at CLH April 1983 - March 1984.

	No. of cases	No. of deaths	Rate (%)
Adults			
Male	14	2	14.3
Female	26	2	7.7
Children			
Male	2	-	-
Female	4	-	1-
Total	46	4	8.7

Table B-3. Clinical diagnosis of 46 LF and Presumptive LF patients treated at CLH April 1983 - March 1984.

Clinical diagnosis	No.
Lassa fever	38
Typhoid fever	3
Sickle cell crisis	1
Severe anemia	1
Pyelonephritis	1
Cerebral malaria	1
Tonsilitis	1
Total	46

Table B-1. Results of serological and virological testing of febrile patients at Curran Lutheran and Phebe Hospitals, Liberia.

Hospital and Dates	No. Tested	Lassa fever: Virus isolation	Lassa fever: Seroconversion Rising LV Titers	Lassa fever: Total No.	Lassa fever: Total (%)	Pre-sumptive LF	Total No.	Total (%)	Other LVA positive
C L H									
03/83-04/83*	57	3	1	4	(6.9)	5	9	(15.5)	3
05/83-11/83	214	9	5	14	(6.5)	4	18	(8.4)	17
12/83-04/84	229	#	22	22	(9.6)	14	36	(15.7)	10
Total	509	12	28	40	(8.0)	12	63	(12.6)	30
PH									
02/82-02/83*	104	4	5	9	(8.7)	4	13	(12.5)	6
03/83	95	#	2	2	(2.1)	8	10	(10.5)	17
Total	199	4	7	11	(5.5)	12	23	(11.5)	12

* Included in Annual Report dated August, 1983 but without results of virus isolations.

\# Virus isolations not attempted at time of this report

Appendix B. Testing of febrile hospital patients for the diagnosis of Lassa Fever.

Virus isolation was attempted in 58 patients at Curran Lutheran Hospital and 104 patients at Phebe Hospital among whom the results of serological tests were reported last year. Both virological and serological techniques were performed on another 214 patients in CLH. Serological tests only were done on sera from 229 patients admitted to CLH with fever, and 95 patients treated at PH. The results of tests are given in Table B-1.

During the year April, 1983, through March, 1984, LF or presumptive LF was diagnosed in 55 patients; virological evaluation has not yet been completed for specimens obtained from about one-half the patients. Clinical information has been forwarded from CLH for 46 of these cases. In Table B-2 the distribution of the patients is presented by age and sex, together with the number of deaths among them.

In Table B-3 the clinical diagnoses at death or discharge are listed for the 46 patients whose clinical information is at hand.

An evaluation of the diagnostic procedures was made of all patients tested at CLH from July, 1980, through November, 1983 in whom both serological and virological tests were performed. The results given in Table B-2 demonstrate that under the conditions at CLH diagnosis of LF by virus isolation was possible in about one-half of patients in whom the diagnosis was eventually made. Seroconversion or a 4-fold rise in antibody titers was present in over two-thirds of patients. High antibody titers diagnostic of presumptive LF was present in nine of 25 patients in whom virus isolation was positive.

Maza	07/82	20 Sep 83	640	0.7	1.0	2	2
		01 Nov 83				2	1
		05 Mar 84	640	0.8	0.7	2	2
		12 Jun 84				2	
Total:						141	59

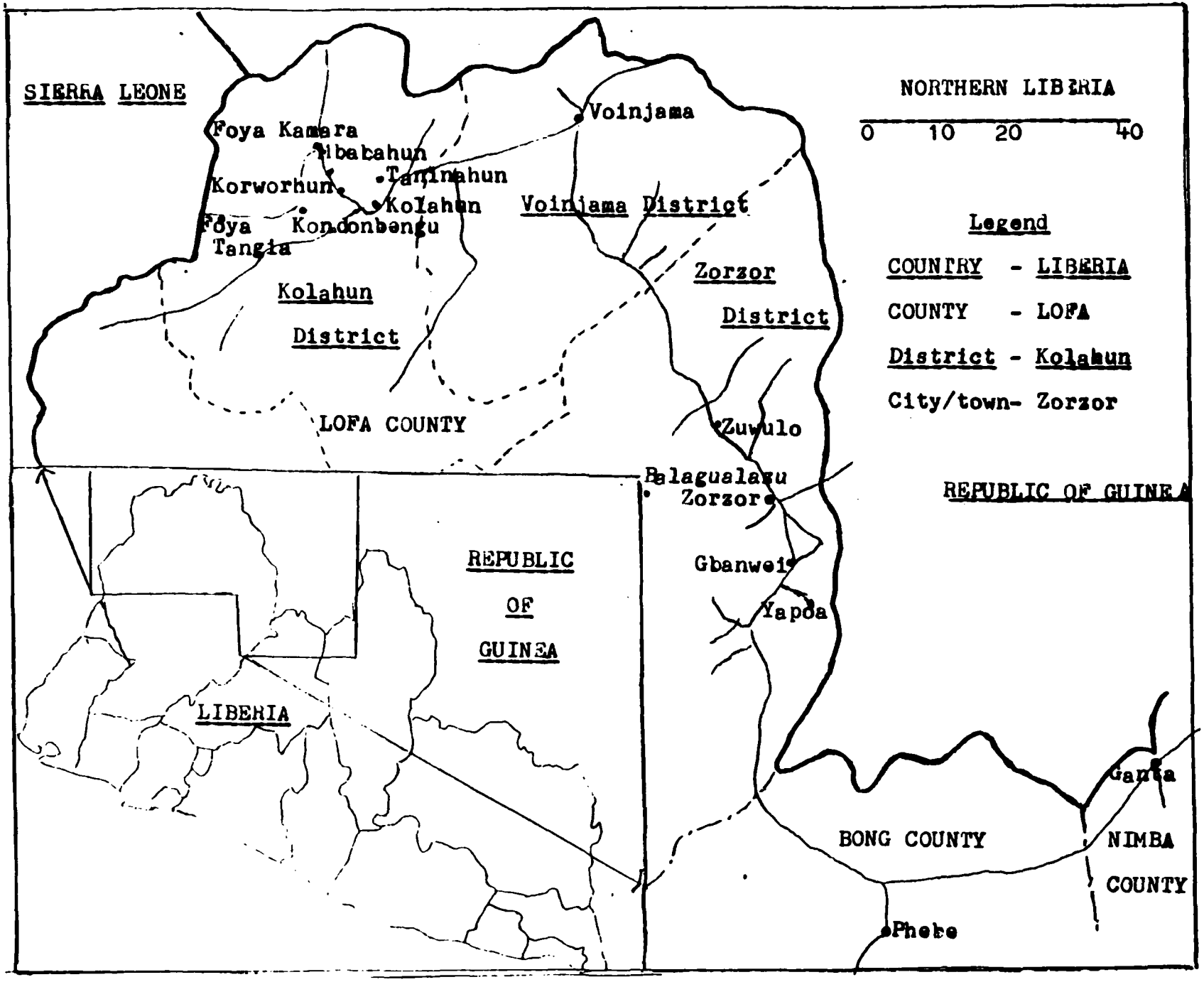
* Expressed as reciprocals

Log neutralization index of the sera when tested against the Josiah (Sierra Leone) and Macenta (Liberia-Guinea) strains of Lassa virus.

KoKo	?	22 Sep 83	80(NS)	1.0	0.9	2	1
		08 Mar 84				2	
GaKo	06/83	31 Oct 83	40	3.4+	3.1+	2	2
MaKa	03/83	16 Dec 83	80	3.6+	3.8+	2	2
NoMa	03/82	13 Jun 84				2	
JaMo	?	31 Oct 83	40(NS)	1.1	1.1	2	2
		16 Dec 83	10	0.6	0.8	2	1
		16 Apr 84	10	1.1	1.1	2	2
		13 Jun 84				2	
CeMu	04/83	14 Dec 83	640	3.6+	3.8+	2	1
		16 Apr 84	320	3.6+	3.8+	2	1
AnSu	09/82	02 Nov 83	1280	3.4+	3.1+	2	1
		08 Mar 84	320	3.6+	3.8+	2	2
DaSu	01/83	23 Sep 83				2	
		01 Nov 83	160	1.2	0.9	2	2
		15 Dec 83				2	
		12 Jun 84				2	
MuSu	11/81	01 Nov 83	40	2.7	3.1	2	1
		07 Mar 84	20	2.0	2.4	2	2
		13 Jun 84				2	
BeTo	?	14 Jun 84				2	
DaTo	03/83	20 Sep 83	80	1.2	1.0	2	1
		02 Nov 83	160	0.6	1.0	2	2
		14 Dec 83	40	0.9	1.1	2	1
		07 Mar 84	40	1.1	1.3	2	2
		13 Jun 84				2	
HuTo	1981	19 Sep 83	80(NS)	0.3	0.4	2	1
GaVa	01/82	19 Sep 83				2	
		01 Nov 83	80(NS)	3.4+	3.1+	2	1
		06 Mar 84				2	
YaVa	01/82	06 Mar 84	20	1.1	1.1	2	1
		13 Jun 84				2	
BeVa	?	21 Sep 83	10-	0.9	0.8	2	1
		16 Dec 83				2	
		16 Apr 84				2	

Appendix A. Lassa Fever Immune Plasma Units Collected in Liberia. August 1983 - July 1984.

Donor	Date of Illness	Date of Donation	IFA Titer*	LNI (neutralization)# Josiah	Macenta	No. of Units Collected	USAMRIID
DaDo	04/77	31 Oct 83	20	0.8	1.0	2	1
		10 Dec 83				2	1
		05 Mar 84	10	0.9	1.0	2	2
		16 Apr 84				1	
		12 Jun 84				2	
KoDo	05/77	21 Sep 83	40(NS)	0.9	0.6	2	1
DaBa	11/82	31 Oct 83	40	1.8	1.4	2	1
		14 Dec 83				2	
		13 Jun 84				2	
PaFl	07/83	16 Dec 83	10	3.6	3.8+	2	2
		26 Apr 84				2	
LoFl	01/82	15 Dec 83				2	
		08 Mar 84				2	
IrJo	02/83	22 Sep 83	80	2.3	2.0	2	1
		16 Apr 84				2	
BoKa	10/82	20 Sept 83				2	
		31 Oct 83	10(NS)	1.1	1.0	2	
		14 Dec 83				2	
		06 Mar 84				2	
		12 Jun 84				2	
KeKa	10/82	19 Sep 83	160	1.9	2.2	2	2
		02 Nov 83				2	
YoKa	08/83	16 Apr 84	2560	3.6+	3.8+	2	2
YoKe	?	14 June 84				2	
YaKo	10/81	16 Apr 84	20	2.4	2.4	2	2
		12 Jun 84				2	
DaKo	10/81	20 Sep 83	320	3.6+	3.8+	2	2
		15 Dec 83	80	3.6+	3.8+	2	2
		05 Mar 84	160	3.6+	3.0	2	
		12 June 84				2	
KeKo	10/81?	21 Sep 83	320	1.3	1.6	2	1
		16 Apr 84	160	2.3	1.4	2	2



MAP -- NORTHERN LIBERIA

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Yalley-Ogunro, J.E., Frame, J.D. and Hanson, A.P. Endemic Lassa fever in Liberia. VI. Village serological surveys for evidence

obtained from their households.

Tables giving the results in greater detail are given in Appendix C.

VI. Conclusion

Plasmapheresis has continued in Liberia at CLH, and at the end of this report year has been started at PH as well. By this time the criteria for the collection of LFIP have become fairly established, and a higher proportion than in the past have been found to have adequate LNI for use in the treatment of LF.

With the new freezer units at CLH and PH treatments of LF patients in these institutions are now being monitored closely to measure the effectiveness of treatment with LFIP, not only on clinical but most specifically on virological grounds. Virological tests are in progress at the time of this report.

Surveys of patients indicate that LF continues as in the past to be an important cause of morbidity in northwestern Liberia; it is found consistently in 10% or more of adult patients admitted to the hospital with fever. It has also been found to be a serious illness among children admitted for hospital care with a mortality of 20% or more among them, and infection of pregnant women is almost universally lethal to the unborn.

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C. Village Surveys

Following up previous investigations of LV activity in Lofa County villages, two more were studied in Kolahun District where the prevalence of LF is known to be high. Both villages were off the main highway, in contrast to two villages in the same district which were surveyed previously. Taninahun is at the end of an access road, while Kondonbengu is on a secondary road from the main highway to Foya Tangia.

The surveys were conducted by Dr. Andrew Cole, and Mr. J.E. Yalley-Ogunro. After agreement from the village chief and elders, the inhabitants were requested to present themselves on the selected date. They were registered by households, and tested by means of finger tip blood collected on filter paper discs; if two discs are used for each subject they will hold at saturation about 0.6 ml. blood. The specimens were dried, stored in a freezer and taken to the LIBR to be tested for the presence of IFA. It has been found that after appropriate dilution the screening titer is approximately 1:8.

Tests were conducted on 236 inhabitants of Taninahun, of whom 4 were positive at the screening of 1:8, and one at a titer of 1:16; 13 gave equivocal results. The prevalence of LVA positive sera was thus 2.1% with definitively positive sera, 7.7% if the questionable reactions are included.

At Kondonbengu 239 people were tested. Two were positive at the screening titer of 1:8, and one each at 1:16, 1:256, 1:512 and 1:2048. Eleven gave questionable results. The prevalence of LVA positive sera was 2.5%, 7.1% if those with questionable reactions are included.

The reactions may be compared with those of two roadside villages tested previously (11). At Mbabahun the prevalence of LVA-positive sera was 4.1%, and at Korworhun, 5.7%. The results parallel those of four villages of Zorzor District tested earlier (3) in which the prevalences of LVA positive sera were higher in the villages near the main road than in those located "in the bush".

The presence of sera with relatively high LVA titers has been assumed to reflect relatively recent LV activity; in Kondonbengu there has apparently been some LV infection in the near past, though specific histories of unusual fever were not elicited from those who were surveyed. In this village there was one household with two sera at titers over 1:8; the other definitely positive reactions in both villages were the only ones in their households. However, if the sera with questionable reactions in Kondonbengu are taken into account, 9 were in households in which there was more than one LVA-positive person. In Taninahun 7 sera were positive or questionably positive in 3 houses, while the other 11 were the only positive specimens

The relative value of virological and serological techniques in the diagnosis of LF has practical significance. The number of laboratories in which virus isolation may be attempted safely is limited. Even in these laboratories which are essentially research institutions and not clinical diagnostic centers the load of arduous virus isolation attempts becomes a serious drain on the time and facilities which might otherwise be used in basic research into the biology of LV.

CLH is a hospital in which the diagnosis of LF is taken seriously, in which attempts to make laboratory diagnosis possible are carried out to the extent that is likely possible in an African hospital with significant constraints in personnel and physical facilities. Between July, 1980, and November, 1983, 673 patients admitted to CLH for treatment of fever were tested by both virological and serological means. Of these, LV was isolated in 42, or 51.2%. In 17 cases virus isolation was the only means of diagnosis; of the other 25, 16 showed diagnostic seroconversion or rising titers of LVA, and 9 had titers of LVA compatible with the diagnosis of "presumptive LF." Serological tests led to the diagnosis of 40 other cases of LF and 28 of presumptive LF. Thus, the serological diagnosis of LF was made in 56 or 68.3% of the 82 cases of LF. Of the total of 110 cases of LF and presumptive LF, virological diagnosis was made in 38.2% of cases and serological diagnosis in 84.5%.

Reasons for the missing of cases of LF by virological techniques appear to include attempts at virus isolation relatively late in the course of illness, and likely, inadequate preservation of LV in the storage of specimens at -20°C. However, if virus isolation had not been attempted 17 patients with LF would have been missed, 20.7% of the 82 cases of LF, 15.5% of LF and presumptive LF cases.

The cause of missing LF by serological tests was the collection of only one serum, or two sera early in the course of illness, either through oversight or because of death or departure of the patient from the hospital before diagnostic LVA titers could develop.

Under the conditions prevailing at CLH one can expect to diagnoses LF and presumptive LF in about 85% of cases by serological means alone; the rate is likely to be higher if careful attention is given to the collection of early and late sera from patients suspected of having LF. This is not to minimize the importance of virus isolation. The technique gives strong corroboration to the results of serodiagnosis, and is important in the investigation of types of LV associated with the varying degrees of morbidity and mortality of LF found in different regions and at various times.

The results of testing patients for LV infection are tabulated in Appendix B.

Table C-2. Prevalence of LVA in inhabitants of four villages in Kolahun District, Lofa County, Liberia, by age and sex.

Village	Age				Total	Rate
	Adult	Adol-escent	5-12 years	Under 5 years		
Males						
Taninahun	1/52	0/8	0/30	0/21	1/111	.9
Kondonbengu	4/49	0/7	0/31	1/26	5/113	4.4
Total males	5/101	0/15	0/61	1/47	6/224	2.7
Females						
Taninahun	3/74	1/18	0/15	0/18	4/125	3.2
Kondonbengu	1/62	0/16	0/27	0/21	1/126	.9
Total females	4/136	1/34	0/42	0/39	5/251	2.3
Total	9/237	1/49	0/103	1/86	11/475	2.3

Table C-3. Comparison of LVA prevalences in highway and off-highway villages, Kolahun District, Lofa County, Liberia.

Villages	IFA Positive	IFA Negative	Total	Rate
Highway				
Mbabahun & Korworhun	28	572	600	.047
Off-highway				
Taninahun & Kondonbengu	11	464	475	.023

$X^2 = 3.54$, P 0.05

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